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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/492,028	01/26/2000	Charles S. Zuker	02307E- 092610	9361

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EXAMINER

BUNNER, BRIDGET E

ART UNIT	PAPER NUMBER
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1647

DATE MAILED: 10/01/2003

29

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Applicati n No.

09/492,028

Applicant(s)

ZUKER, CHARLES S.

Examiner

Bridget E. Bunner

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 July 2003.
- 2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3,4 and 6-8 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3-4,6-8 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 28 July 2003 (Paper No. 28) has been entered in full. Claim 1 is amended and claims 2, 5, and 9-24 are cancelled.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1, 3-4, and 6-8 are under consideration in the instant application.

Specification

1. The objection to the specification regarding the issue of patent applications being referenced throughout the disclosure is maintained and held in abeyance until allowable subject matter is identified. This objection will be maintained until the referenced application (09/361,652) is abandoned or allowed or if the instant application is deemed allowable.

Claim Rejections - 35 USC § 112

2. Claims 1, 3-4 and 6-8 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The basis for this rejection is set forth at pg 3-8 of the previous Office Action (Paper No. 26, 12 February 2003).

Specifically, claims 1, 3-4 and 6-8 are directed to a method for identifying a compound that modulates signal transduction in taste cells, comprising the steps of (i) contacting a cell which expresses a taste cell specific G-protein alpha subunit polypeptide and a taste cell specific G protein coupled receptor with the compound, the G-protein alpha subunit polypeptide

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comprising greater than 90% amino acid sequence identity to a polypeptide having a sequence of SEQ ID NO: 2, wherein the G-protein alpha subunit polypeptide is a subunit of a heterotrimeric G-protein which binds GTP; and (ii) determining a functional effect of the compound upon the cell expressing the taste cell specific G-protein alpha subunit polypeptide and the taste cell specific G protein coupled receptor, thereby identifying a compound that modulates signal transduction in taste cells. The claims also recite that the functional effect is determined by measuring increased or decreased binding of radiolabeled GTP to the G-protein alpha subunit polypeptide or to a G protein comprising the G-protein alpha subunit polypeptide. The claims recite that the that G-protein alpha subunit polypeptide comprises an amino acid sequence of SEQ ID NO: 2 and is expressed in a cell or a cell membrane.

Applicant's arguments (Paper No. 28, 28 July 2003), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

Applicant asserts that identification and use of polypeptides having 90% of greater percent identity to SEQ ID NO: 2 is well within the abilities of one of skill in the art, with at most routine experimentation. Applicant also argues that the claims have been amended to specify a functional element, in which the G-protein alpha subunit polypeptides "is a subunit of a heterotrimeric G-protein which binds GTP". Applicant contends that the specification provides assays in which one of skill, only with routine experimentation, can determine operable embodiments of the invention, such as binding of radiolabeled GTP to the G-protein.

Applicant's arguments have been fully considered but are not found to be persuasive. Furthermore, although the specification in the instant application teaches art-recognized procedures for producing and screening for active muteins, this is not adequate guidance as to the

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nature of active G-protein alpha subunit polypeptide derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. The skilled artisan must resort to trial and error experimentation to generate the infinite number of variants and fragments of G-protein alpha subunit polynucleotides and polypeptides, as recited in the claims and to screen them for a desired activity (e.g., forming a heterotrimeric G-protein which binds GTP). Such trial and error is considered undue.

Additionally, the broad brush discussion of making and screening for G-protein alpha subunit variants does not constitute a disclosure of a representative number of members. No such variants were made or shown to have activity. Only the G-protein alpha subunit nucleic acid sequence of SEQ ID NO: 1 and the amino acid sequence of SEQ ID NO: 2 are disclosed. The specification's general discussion of making and screening for variants constitutes an invitation to experiment by trial and error.

The Examiner acknowledges that it is not a function of the claims to specifically exclude possible inoperative embodiments, and the presence of inoperative embodiments within the scope of a claim does not preclude enablement of the claim. However, the scope of the claim may still not be enabled where undue experimentation is involved in determining those embodiments that are operable. MPEP § 2164.08(b) states that "claims reading on significant numbers of inoperative embodiments would render the claims nonenabled when the specification does not clearly identify the operative embodiments and undue experimentation is involved in determining those that are operative.

Furthermore, the specification of the instant application outlines a prophetic procedure for screening a compound that modulates signal transduction in taste cells. However, this is not

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adequate guidance, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. The specification of the instant application does not disclose the identity of any substance capable of modulating signal transduction in taste cells via the claimed method. Since the specification provides no guidance regarding what sort of compounds should be screened for the desired activity, the skilled artisan must resort to trial and error experimentation to determine which class of compounds might yield one with the desired activity. Such trial and error experimentation is considered undue. Therefore, undue experimentation would be required of the skilled artisan to contact a cell which expresses numerous possible variants of a G-protein alpha subunit polypeptide of SEQ ID NO: 2 and any taste cell specific G protein coupled receptor with any type of compound. There is also little guidance in the specification or the claims indicating which taste cell specific G protein coupled receptor is expressed or whether the G-protein alpha subunit polypeptide and the taste cell specific G protein coupled receptor are endogenous to the taste cell or are transfected into the taste cell. Additionally, as was found in Ex parte Hitzeman, 9 USPQ2d 1821 (BPAI 1987), a single embodiment may provide broad enablement in cases involving predictable factors such as mechanical or electrical elements, but more will be required in cases that involve unpredictable factors such as most chemical reactions and physiological activity. See also In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970); Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 927 F.2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed. Cir.), cert. denied, 502 U.S. 856 (1991). The present invention is unpredictable and complex wherein one skilled in the art may not necessarily identify a compound that modulates signal transduction in taste cells. Although the claimed method utilizes routine screening techniques, the results of the method are unpredictable and

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complex when combined with the step of contacting a cell which expresses *any* taste cell specific G-protein alpha subunit polypeptide derivative of SEQ ID NO: 2 *and* any taste cell specific G protein coupled receptor with *any* compound.

Proper analysis of the Wands factors was provided in the previous Office Action. Due to the large quantity of experimentation necessary to identify a class of compounds to put into contact with a taste cell, to generate the infinite number of polypeptide derivatives recited in the claims and possibly screen same for activity, and to modulate signal transduction in taste cells with numerous G-protein alpha subunit polypeptide variants and any taste cell specific G protein coupled receptor, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide G-protein alpha subunit polypeptide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any specific taste cell specific G protein coupled receptors or structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Conclusion

No claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (703) 305-7148. The examiner can normally be reached on 8:30-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 872-9305.

BEB
Art Unit 1647
26 September 2003

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER